REMARKS

The Office Action has been carefully studied. No claim is allowed. Claims 3 and 17-22 presently appear in this application, with claims 21 and 22 being newly added, and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 3 and 17-20 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner finds the specification, while being enabling for the claimed method wherein the proliferated transformed tumor cells produced *ex vivo* in claim 3 or claim 17 are directly administered into a tumor of a subject to treat the tumor cells of the tumor in the subject, does not reasonably provide enablement for transplanting the proliferated tumor cells at any site in the subject. This rejection is obviated by the amendments to claims 3 and 17 to positively recite that the proliferated transformed tumor cells are transplanted into a tumor of the subject.

The rejection is discussed below as it might relate to new claims 21 and 22, which are supported by the specification at page 11, second paragraph to page 12, first paragraph, and the state of the art at the time the present invention was made.

In the outstanding rejection for lack of enablement, the examiner held that:

(a) the methods disclosed in Goto et al. "Gene Therapy", vol. 7, page 1, 672-1, 679 (2000) and Ju et al., "Gene Therapy" 2000, both submitted by the applicants, are not "*ex invo* therapy";

(b) the vector and administration method of the vector disclosed in Goto et al. are different from those of the present invention;

(c) Goto administers an adenoviral vector; and

(d) Therefore the Goto and Ju references do not provide enabling support for the claimed invention.

Applicants believe, however, that Goto and Ju do indeed provide enabling support for new claims 21 and 22. A copy of U.S. Patent 5,358,866, issued October 5, 1994, is attached hereto to show the state of the art at the time the present invention was made. From the content of U.S. Patent '866, it is clear that gene therapy, i.e., "*ex vivo* therapy" has been conducted at the time the present invention was made (see "Abstract" and column 7, lines 23-43). It is therefore believed that one of skill in the art would have easily understood the usefulness and the enablement of the claimed invention based on the state of the art such as disclosed in U.S. Patent '866 and the disclosure of the present specification.

Furthermore, with respect item (b) above, it should be noted that the vectors, such as the retroviral and adenoviral vectors used in Goto (see page S36, left column) are also used in the present invention (instant specification, page 11, line 9). Goto, at S35, right column, lines 2-8 from the bottom, states as follows:

> Therefore, in our previous study we fused a signal sequence derived from human PTH(10) to the 5' end of mature IL-18 cDNA to construct vectors capable of expressing bioactive IL-18 and demonstrated that direct injection of an IL-18 adenoviral vector (Ad.PTH.IL-18) into tumor elicited potent antitumor effects.

With respect to item (c) above, it should be noted that the reason why Goto uses an adenoviral vector is to enhance the effectiveness of gene therapy. In fact, Goto states from page S35, right column, line 2 from the bottom to page S36, left column, line 2, as follows:

> Increased amount of IL-18 secretion appears to be necessary to achieve better antitumor effects. In this study, the leader sequence of the IL-1ra was ligated to the to the IL-18 gene to improve production of IL-18 secretion.

In other words, Goto never implies that gene therapy is only effective if an adenoviral vector is used.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

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Respectfully submitted,

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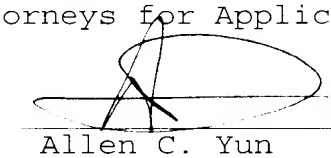
By 
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